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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,071	03/17/2005	Cristiano Alberto Ribeiro Santana	P08596US00/BAS	2669

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,071	SANTANA ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 7-19-05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed March 17, 2005, has been received and entered.

Claims 1-20 are pending and examined on the merits.

Claim Objections

Claims 1-14 are objected to because of the following informalities: The claims use French terms. Specifically, "bromeline" should be replaced with "bromelain," "vitamine E" should be replaced with "vitamin e," and "papaine" should be replaced with "papain." Claim 7 is also objected to since the dash sign in the phrase "Vitamine-E," should be removed. Finally, claims 4-8 and 14 are objected to because each do not end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 15 and 18 are rendered indefinite by the recitation "lyophilized." The claim recites that the composition is "...presented in the form of a..." but goes on to state that one of the forms is a "lyophilized." The term "lyophilized" is an adjective and not a form. Thus, claims 15, 16, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 5, 9, 10, and 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bilton (WO 84/02846).

Bilton discloses a topical ointment for skin surface wounds comprising enzymes and carriers such as emollient oils and polyhydric alcohol emollient (abstract). The Bilton compositions comprise one or more proteolytic enzymes, including papain and bromelain (page 5, lines 12-15). One of the ointments claimed by Bilton comprises about 0.1 to 2% papain, and about 0.1 to 2% bromelain (claim 9), thus the claimed invention is anticipated.

A holding of anticipation is clearly required.

Claims 1-4 and 13-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Santana et al. (WO 01/70258).

Santana et al. discloses a pharmaceutical composition comprising carriers for products and bromelain at a concentration of more than 0.1% or 0.5 to 5%, hyaluronidase at a concentration of 50 to 900 utr/mg, and vitamin E at a concentration of 10 to 2000 mg (claims 1 and 2). Furthermore, Santana et al. states that the composition is applicable under any form, including a gel, cream, liquid, spray, and aerosol (page 1, lines 4-8).

A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5, 6, and 9-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petereit et al. (US 4,904,469).

Petereit et al. discloses a wound covering comprising non-immobilized enzymes for wound therapy. The wound covering comprises a variety of enzymes, including hyaluronidase (column 3, line 19), and proteases including papain and bromelain (column 3, lines 23-27). Claim 2 of the Petereit invention recites that the wound covering, which is for topical skin treatment, comprises of a mixture of proteases and hyaluronidases.

Petereit et al. differs from the claimed invention in that it does not disclose the concentrations of the bromelain, papain, and hyaluronidase in the composition. Nevertheless, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have varied the concentration of each enzyme in the Petereit wound covering. One of ordinary skill in the art would have been motivated to do this since the selection of appropriate enzyme concentrations would have been a routine matter of optimizing a result-effective parameter at the time of applicant's invention, as the effect on a wound would differ according to the concentration of each of the enzymes. Thus, a holding of obviousness is clearly required.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilton in view of Klock et al. (WO 99/46368) and Ismail (US 5,786,384).

As discussed above, Bilton anticipates claims 1, 2, 5, 9, 10, and 15-20. However, Bilton does not expressly disclose that ointment for skin wounds further comprises hyaluronidase or vitamin E in combination with bromelain and papain.

Klock et al. discloses "...a method for treating wounds comprising the step of administering an effective amount of a carbohydrate-active enzyme" (abstract). The carbohydrate-active enzyme can be hyaluronidase (page 11, fifth paragraph). The enzyme can

be applied by topical cutaneous administration (page 7, third paragraph), where the composition comprising the enzyme can comprise carrier material (page 9, second paragraph).

Ismail discloses that vitamin E and a combination comprising vitamin E together with other active substances are suitable as agents for the treatment of wounds (column 2, lines 11-16). The Ismail invention is a method for the treatment of human and animal skin wherein vitamin E is administered to the skin (column 2, lines 32-40). The dosage of vitamin E should be in the range of from 200 to 1,000 mg, and preferably 250 to 600 mg (column 2, lines 56-62).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have further included hyaluronidase and vitamin E in the Bilton ointment comprising bromelain and papain. One of ordinary skill in the art would have been motivated to do this because it is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Given that both hyaluronidase and vitamin E are used in ointments for the treatment of wounds, it would have been obvious to have combined it with the Bilton ointment which serves the same purpose.

Ismail teaches a composition comprising a quantity of vitamin E which is within the range recited in the instant claims. Even if this were not disclosed, it is noted that the amount of vitamin E recited in applicant's claims depends on the absolute amount of composition present.

The references discussed above differ from the claims under examination in failing to disclose the activity of hyaluronidase recited in the claims. However, the artisan of ordinary skill in the art would have recognized that varying the activity of hyaluronidase would have affected the properties of the resulting composition. Thus, the artisan of ordinary skill would have considered the determination of suitable activities of hyaluronidase the optimization of a result-effective parameter, and therefore obvious under §103(a). Absent some unexpected result coming from the claimed activity of hyaluronidase, the usage of activities expected to function in accordance with the cited prior art must be considered *prima facie* obvious.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santana et al. (US 2003/0049247 or WO 01/54647) in view of Bilton.

Santana et al. discloses a pharmaceutical composition comprising carriers and papain at 0.2 to 15%, hyaluronidase at 50 to 900 utr/mg, and vitamin E at 10 to 2000 mg (claim 1 of `247 and `647). The Santana composition is used in any pharmaceutical form, including a "...gel, cream, aerosol and spray, liquid and liophilizated" and can be topically applied (page 1, paragraph [0001] of `247 and page 1, lines 4-9 of `647). Additional substances that can be included in the pharmaceutical composition include an anti-inflammatory (page 3-4, paragraphs [0035]-[0048], particularly paragraph [0044] of `247 or page 19, lines 1-17, particularly line 13 of `647). Santana et al. differs from the claimed invention in that it does not disclose that the pharmaceutical composition also comprises bromelain.

Bilton discloses a topical ointment for skin surface wounds comprising enzymes and carriers such as emollient oils and polyhydric alcohol emollient (abstract). The Bilton

compositions comprise one or more proteolytic enzymes, including papain and bromelain (page 5, lines 12-15). One of the ointments claimed by Bilton comprises about 0.1 to 2% bromelain (claim 9). Finally, Bilton points out that proteolytic enzymes such as bromelain are anti-inflammatory agents (page 5, lines 5-12 and page 6, lines 29-32).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have included bromelain in the Santana composition, at the concentration recommended by Bilton. One of ordinary skill in the art would have been motivated to do this since bromelain would have served as an anti-inflammatory agent in the Santana composition. As discussed above, Santana et al. points out that their composition can further include additional agents, including anti-inflammatory agents. Thus, a holding of obviousness is clearly required.

Claims 1-3, 5, 6, and 9-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gokcen (WO 90/08555).

Gokcen discloses a composition comprising a pharmaceutically acceptable aqueous carrier solution comprising two or more hydrolytic enzymes, which include hyaluronidase, bromelain, and papain (claims 2 and 3) for the treatment of prostatic hypertrophy (thus the composition is used for the production of a medicine).

Gokcen differs from the claimed invention in that it does not disclose the concentrations or activities of the enzymes as claimed. Nevertheless, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have varied the concentration/activity of each enzyme in the Gokcen invention. One of ordinary skill in the art would have been motivated to do this since the selection of appropriate enzyme

concentrations/activities would have been a routine matter of optimizing a result-effective parameter at the time of applicant's invention, as the effect on prostatic hypertrophy would differ according to the concentration of each of the enzymes.

Although Gokcen does not specifically teach that the composition is applied either dermically or transdermically, the products are the same, thus the claimed function must be inherent to the reference composition. The discovery of a previously unappreciated use of a prior art product does not render the old product patentably new. As pointed out in MPEP §2112, "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Thus, a holding of obviousness is clearly required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/182,265 in view of Bilton (WO 84/02846).

The claims of the instant application differ from the claims of the copending application in that the instant claims require that the composition contain bromelain. However, Bilton teaches a pharmaceutical composition comprising papain along with bromelain (abstract), and points out the proteolytic enzymes such as bromelain are anti-inflammatory agents (page 5, lines 5-12 and page 6, lines 29-32). Application `265 requires that a composition comprising papain, hyaluronidase, and vitamin E comprise a pharmaceutically active substance (claim 3), and that the pharmaceutically active substance may be an anti-inflammatory (claim 19). Given the teachings of Bilton, the person of ordinary skill in the art would have recognized the suitability in using bromelain as the anti-inflammatory agent in the `265 composition, at the concentration disclosed in Bilton.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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